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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/714,767	11/16/2000	Dennis L. Bidney	35718/201902	5068

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EXAMINER
KALLIS, RUSSELL

ART UNIT	PAPER NUMBER
1638	17

DATE MAILED: 06/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/714,767	BIDNEY ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4 and 25-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4 and 25-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/17/03 has been entered.

Claims 2-4 and 25-46 are pending.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: An isolated polynucleotide from Sunflower encoding a protein with LOX activity.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2-4, 25-26 and 32-46 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for

the reasons of record set forth in the Official actions mailed 7/23/2002. Applicants arguments filed October 23, 2002 and March 17, 2003 have been considered but are not deemed persuasive.

Applicant broadly claims an isolated nucleic acid having 90% sequence identity to SEQ ID NO: 3, or that hybridizes under highly stringent conditions to SEQ ID NO: 3, or comprises at least 200 consecutive nucleotides of SEQ ID NO: 3, wherein said nucleic acid molecule encodes a polypeptide having LOX-like activity.

Applicant describes a single nucleic acid molecule (SEQ ID NO: 3).

Applicant does not describe any DNA sequences with 90% sequence identity to SEQ ID NO: 3, or DNA sequences that hybridize under highly stringent conditions to SEQ ID NO: 3, or comprise at least 200 consecutive nucleotides of SEQ ID NO: 3; and encode a polypeptide having LOX-like activity. Therefore, Applicant does not provide an adequate written description of the claimed invention, and it is unclear if Applicant was in possession of the invention as broadly claimed. Claims 32-36 are included in the rejection because Applicant has not met the deposit requirements.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The court also addressed the manner by which genus of cDNAs might be described: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a

recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.* At 1406.

5. Applicant asserts that recitation of a sequence having 90% sequence identity is a very predictable structure (response page 7), is sufficient to satisfy the written description requirement (response page 8) and when correlated with function i.e. a LOX-like activity, as a limitation recited in the claims the genus is sufficiently described (response page 8). Applicant's description of the single nucleic acid molecule of SEQ ID NO: 3 does not provide for an adequate written description of a representative number of nucleic acid molecules of the claimed genus.

Applicant asserts that amending Claim 42 to recite 200 consecutive nucleotides rather than 50 consecutive nucleotides that encode a polypeptide having LOX-like activity overcomes the previous rejection of Claims 42-46 for lack of written description (response page 8). Applicant's claim with respect to 200 consecutive nucleotides is not supported in the specification by description of any fragments of 200 consecutive nucleotides which encode an active LOX-like polypeptide.

Applicant asserts that Example 15 of the Written Description Guidelines with respect to an antisense oligonucleotide parallels the limitation of 200 consecutive nucleotides encoding a polypeptide having LOX-like activity recited in Claims 42-46 in that the claimed sequence represents a member of the claimed genus and the claims recite functional characteristics of the claimed invention (response page 9). Applicant's claim of 200 consecutive nucleotides encoding a polypeptide having LOX-like activity is not described in the specification and the prior art does not support such a structure having the claimed function of the invention. Furthermore,

Applicant's comparison to antisense oligonucleotides is considered outside the scope of a polynucleotide of at least 200 consecutive nucleotides encoding a polypeptide having LOX-like activity and therefore non-responsive to the Examiner's rejection.

6. Claim 32-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for the reasons of record set forth in the Official actions mailed 7/23/2002. Applicants arguments filed October 23, 2002 and March 17, 2003 have been considered but are not deemed persuasive.

It is apparent that the nucleotide sequence of Accession No. PTA-287 is required to practice the claimed invention. The specification does not provide a repeatable method for obtaining the nucleotide sequence of Accession No. PTA-287 and it does not appear to be readily available material. Without a publicly available deposit of the above, one of ordinary skill in the art could not be assured of the ability to make the invention in the same manner as claimed. Given the lack of guidance in the specification and inability of those in the art to reproduce specific DNA sequences, it would require undue experimentation for one skilled in the art to identify and obtain the nucleotide sequence of PTA-287. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of SEQ ID NO: 3. See 37 CFR 1.802.

Deposit of the nucleotide sequence of Accession No. PTA-287 would satisfy the enablement requirements of 35 U.S.C. 112, first paragraph.

If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If the deposit was not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the following criteria have been met:

(a) during the pendency of this application, access to the deposits will be afforded to one determined by the commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in the public depository for a period of at least thirty years from the date of the deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposits will be replaced if they should become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification. In addition, the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.801 - 1.809 [MPEP 2401-2411.05] for additional explanation of these requirements.

Applicant asserts that they have chosen to explicitly state each requirement of the deposit under 37 CFR 1.808 instead of indicating that the deposit was made under the terms of the Budapest treaty as stated in MPEP 2408. Applicant states that the deposit of 7/32/02 expressly indicates all of the required terms outlined in 37 CFR 1.806 (response page 10).

Although Applicant has chosen to explicitly state each requirement of the deposit under 37 CFR 1.808 instead of indicating that the deposit was made under the terms of the Budapest Treaty, Applicant has not satisfied the deposit requirements. (See 37 CFR 1.808). Applicant's attention is drawn to page 2, of the declaration filed June 26, 2002 (June 23, 2002), section 5(b) to the 'or'. The correct phrasing of the term limitations of the deposit should use an 'and'. A resubmission of a declaration under C.F.R. under § 1.802 is required.

> **§ 1.806 Term of deposit.**
> A deposit made before or during pendency of an application for patent shall be made for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposit was received by the depository. In any case, samples must be stored under agreements that would make them available beyond the enforceable life of the patent for which the deposit was made.

7. Claims 2-4, 25-46 remain rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to the sunflower nucleic acid molecule of SEQ ID NO: 3 or the deposit thereof as Accession No. PTA-287, and that encodes a polypeptide having LOX activity; a DNA construct comprising said nucleic acid molecule operable linked to

a promoter and a transformed host cell comprising said DNA construct. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official actions mailed 7/23/2002. Applicants arguments filed October 23, 2002 and March 17, 2003 have been considered but are not deemed persuasive.

Applicant broadly claims an isolated nucleic acid having 90% sequence identity to SEQ ID NO: 3, or that hybridizes under highly stringent conditions to SEQ ID NO: 3, or comprises at least 200 consecutive nucleotides of SEQ ID NO: 3, wherein said nucleic acid molecule encodes a polypeptide having LOX-like activity.

Applicant teaches PCR based RACE isolation of a full length cDNA (SEQ ID NO: 3) from Sunflower by RNA profiling of *Sclerotinia* infected sunflower tissue, and teaches by BLAST analysis that the cDNA has sequence identity to a potato, tomato, rice, and *Arabidopsis* nucleic acid molecules that putatively encode lipoxygenase (LOX) (Example 1 page 57, lines 14-23). Applicant teachers that Northern analysis of mRNA levels in sunflower tissue induced with Jasmonic acid or induced by wounding showed an increase in the steady state level of putative LOX mRNA (Example 2 page 61, lines 10-22 and pages 62-63 lines 25-31 and lines 1-4); Applicant provides general guidance for a method of transformation of immature maize embryo using *Agrobacterium* or a biolistic method (Example 3); a method of sunflower meristem explant transformation and regeneration using *Agrobacterium* or a biolistic method (Example 5); and a method of soybean somatic embryo transformation using *Agrobacterium* or a biolistic method (Example 6).

Applicant does not teach the enzymatic activity of the protein encoded by SEQ ID NO: 3 and Applicant does not teach how to use the nucleic acid of SEQ ID NO: 3, DNA sequences with 90% identity to SEQ ID NO: 3, or DNA sequences that hybridize under highly stringent conditions to SEQ ID NO: 3, or DNA sequences that comprise at least 200 consecutive nucleotides of SEQ ID NO: 3; and encode a polypeptide having LOX-like activity.

Isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2).

Further, the isolation of orthologous DNA sequences from other species introduces an element of unpredictability. The limitation is introduced in finding homologous regions that would adequately enable either PCR amplification or southern hybridization and would entail using either degenerate primers or probes with limited sequence identity. Thus the screen for orthologous sequences would isolate many genes other than those of interest. The inherent unpredictability in isolation of a homologous sequence encoding the same protein activity is

illustrated in an example where a small number of changes to the coding region for a strict desaturase resulted in an enzyme with a hydroxylase activity and that a small number of changes to the coding region of a desaturase could account for the functional divergence seen across a range of enzymes involved in fatty acid metabolism (Broun P. *et al.* Science Vol. 282; 13 November 1998, pp. 1315-1317; Abstract lines 4-6 and p. 1317 column 1, lines 37-56).

Furthermore, making a protein that has LOX-like activity and comprises at least 200 consecutive nucleic acids of SEQ ID NO: 3 is not routine in the art. It is well known that proteins are composed of interacting domains many of which translating a mechanism of action through single or groups of amino acid interactions between domains within the protein, or interactions of amino acids with substrate or other proteins. Clearly one cannot predict, even with knowledge of conserved domains, which groups of residues or domains of a polypeptide could be removed from the structure and still preserve detectable enzymatic activity.

The isolation of a nucleic acid having 90% sequence identity to SEQ ID NO: 3, or that hybridizes under highly stringent conditions to SEQ ID NO: 3, or comprises at least 200 consecutive nucleotides of SEQ ID NO: 3; wherein said nucleic acid molecule encodes a polypeptide having LOX-like activity would require making and testing of PCR primers or probes for PCR mutagenesis, PCR isolation, or southern hybridization, to isolate a multitude of non-exemplified DNA encoding a protein with an ambiguous LOX-like activity for transformation of host cells.

Moreover, the specification is speculative about the specific role of the isolated nucleic acids of the invention, the Examples are prophetic with respect to transgenic plants transformed

with said sequences, and the induction of the message only correlates the claimed nucleic acid with wounding and does not teach any causal relationship in preventing disease.

Given the lack of guidance, the absence of working examples in the specification that reflect the breadth of the claims, and the unpredictability in the art, undue trail and error would be needed to practice the invention. Therefore, the invention is not enabled throughout the broad scope of the claims

Applicant asserts that the specification provides sufficient guidance to enable the genus of sequences encompassed by the claims by means of variance to specific structural parameters i.e. 90% sequence identity, hybridization to SEQ ID NO: 3, and possession of at least 200 contiguous nucleotide sequences of SEQ ID NO: 3 and comprising LOX like activity (response page 12). Applicants further assert that the amount of experimentation required to enable the invention is routine and that all the methods needed to practice the invention were well known to those of skill in the art (response pages 12-13). Applicant does not disclose which residues of the polynucleotide sequence are enabling for the invention, i.e. a tangible DNA sequence having 90% sequence identity to SEQ ID NO: 3 and encoding a LOX-like activity.

Applicants asserts (response page 13) that the Broun *et al.* reference teaches away from making substitutions that conserve function of the LOX polypeptide because it teaches substitutions that are not conservative and that the location of the substituted residues is strictly conserved among oleate desaturases. However, this teaching of Broun only highlights the enablement rejection, namely that Applicant has not taught those residues that should be avoided when making changes conservative or otherwise. Since Applicant has not taught which

sequences of SEQ ID NO: 3 when changed would conserve LOX activity the invention is not enabled.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 2-4, 25-26 and 32-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in the rejection.

At Claim 2, line18, and in subsequent claims, "LOX-like activity" is indefinite. It is unclear whether the polypeptide has LOX activity or not.

10. Claims 2-4 and 25-46 are deemed free of the prior art given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide having at least 90% sequence identity to SEQ ID NO: 3 encoding a protein having LOX-like activity and vectors and cells thereof.

11. All Claims are rejected.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the receptionist, whose telephone number is (703) 308-0196.

Russell Kallis Ph.D
May 22, 2003

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600